PATENT SPECIFICATION

(11) 1 425 407

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(21) Application No. 20653/73 (22) Filed 1 May 1973
(31) Convention Application No. 254 897 (32) Filed 19 May 1972 in
(33) United States of America (US)
(44) Complete Specification published 18 Feb. 1976
(51) INT CL² C08L 39/06; A61K 9/52//(C08L 39/06, 31/04)
(52) Index at acceptance
C3P 11D2A1B 11K4 4D3B1 4K11 D9AX D9D4 D9DX E2 PC12A PC12X PC13A PC13B PC14A PC14B PC17 PC18 PC20A PC20B PC20C PC20D1 PC20D2 PC5 PC7 PC8B
A5B 754 757 75Y 764

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(54) IMPROVEMENTS IN OR RELATING TO POLYMERIC N-VINYL LACTAM COMPOSITIONS

(71) We, GAF CORPORATION, a corporation duly organized and existing under the laws of the State of Delaware, United States of America, of 140 West 51st Street, New York, New York, United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to novel compositions of matter. More particularly it relates to improved pharmaceutical preparations providing for the release of pharmacologically active materials over a controlled extended period of time, methods of producing such preparations and stable aqueous emulsions derived therefrom.

~~It has now~~ been found that a pharmaceutical oral dosage may be prepared in such a way as to enable the pharmacologically active material contained therein to be released on contact with the skin or to enable the active material contained therein to be released from the embedded media or emulsion on ingestion at a retarded rate, ~~thus prolonging the phar-~~macological activity and, at the same time, making it possible to control accurately the level of pharmocologically active material in the system so as to provide the desired effect. Among the inert components which are presently being used for such purposes are high molecular weight waxes, used singly or in various combinations, either evenly distributed among the active ingredients or first melted and then carefully coated over small particles of the active components (USP 2,918,411).

One disadvantage in the use of a wax for long-acting tablet formulations is that a relatively large mass of wax must be incorporated in the dosage form to give the desired long-acting effect. In other words, the ratio of wax to active component is a several-fold factor, thus requiring the manufacture of a bulky tablet such that its ingestion by patients is relatively difficult and uncomfortable.

It can be readily seen, however, that one of the prevailing problems in the pharmaceutical development field is the manufacture of controlled-release dosage forms which contain inert components that have large surface area, are nonabsorbable, or if absorbable, are substantially devoid of toxicity and undesirable side effects.

The use of alkaline earth metal salts of saturated fatty acids in tablet manufacture is known. These substances have been used for many years as tablet lubricants and fillers; they are incorporated into the final tablet granulation just prior to compression in relatively small quantities in order to facilitate compression of the granules without their adherence to the punches and dies in the tableting machine.

It is also known that saturated fatty acids, their esters, ethers and alcohols, can be pelletized with polyvinylpyrrolidone by converting the polymer, in the presence of the saturated fatty acid or its derivative, into a molten mass, granulating the congealed mass, reheating, cooling, adding the therapeutic component and palletizing at a temperature near the set point.

It has now been surprisingly found that following the teachings of the present invention, foods which are subjected to heat treatment in processing with an accompanying decrease in nutritive value due to partial or complete loss of carbohydrates, essential amino acids and vitamins may now be processed without losses. As is known, in order to compensate for the aforementioned losses, many nutritive components are added to food before processing is completed. Thus, most canned foods, evaporated milk products, dried protein products, cereals and the like are fortified with amino acids, vitamins, etc. Some of these fortifying agents, however, are them-

(fatty acid PVP) ratio emulsion

selves affected by long periods (sterilization), light, moisture, oxygen or temperature of the environment.

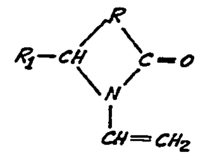
Among the many disadvantages in using saturated fatty acids or their derivatives in combination with polyvinylpyrrolidone to prepare prolonged action dosage unit forms is their physical similarity to high molecular weight waxes. Because of their physical character, large quantities of the saturated fatty acid substance must be employed to obtain a desired effect. Thus, the proportion of polyvinylpyrrolidone to saturated fatty acid material must be about 1.7, or less. Moreover, it is known that saturated fatty acids themselves are inadequate as long-acting vehicle agents, even though combined with polyvinylpyrrolidone. Thus, it has been equally necessary in order to obtain the desired prolonged effect, to incorporate a quantity of high molecular weight waxes, candelilla wax, bees wax or the like in the formulation. This adds further to the bulkiness of the dosage form unnecessarily increasing the volume of the total mass and making the ingestion of same that much more difficult.

On the other hand, by using saturated fatty acid salts, while it is possible to decrease the ratio of salt to polyvinylpyrrolidone, one encounters the problem that there is an absence of complexing between the salt and the polyvinylpyrrolidone. This inherent drawback is immediately obvious where one seeks to produce an emulsion containing active ingredients, polyvinylpyrrolidone and a water insoluble hydrophobic chain end.

It is accordingly an object of the present invention to obviate or minimise one or more drawbacks of the prior art.

According to the present invention there is provided a composition comprising by weight:

(a) 40 parts to 80 parts of a polymer, the polymer comprising (1) a homopolymer of an N-vinyl lactam of the general formula:



wherein R represents an alkylene radical of 2 to 4 carbon atoms and R_1 represents either hydrogen or an alkyl group, or (2) a copolymer of the said N-vinyl lactam with up to 70 percent vinyl acetate based on the weight of the said copolymer;

(b) 60 to 20 parts of a plasticizer;

(c) 0.05 to 50 parts of a medicinally active ingredient and

(d) 0 to 99 parts of solvent for components (a), (b) and (c).

Preferably the composition is one which becomes molten at 100°—150° C. According to another aspect of the invention we provide a stable aqueous emulsion derived from the said composition of the invention.

The compostiion may be formed by heating components (a), (b) and (c) with or without component (d) to form a molten mass and thereafter allowing the mass to cool. Alternatively the composition may be formed by heating component (a) and thereafter adding components (b) and (c) and optionally (d). In the process the heating may be carried out at a temperature of 100°—150° C.

The composition may also be prepared by heating component (b) and adding thereto components (a) and (c) and optically (d) to form a melt mass and thereafter allowing the said mass to cool. An emulsion may thereafter be made from the thus formed composition.

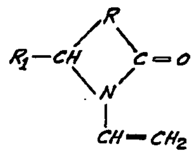
The composition may be used in emulsion or in melt blend form, i.e.,

Melt Blend	Emulsion
Pharmaceutical pill	Milk of magnesia
Suppository	Opacified Soap
Lozenge	Opacified cosmetic
Hair treating composition	Silicone cream
Cosmetic stick	TiO_2 white shoe dressing
Absorbable surgical filament	Insecticidal Spray
	Windshield antifog
	Autopolish
	Liniment
	Cosmetic creme cold cream
	Cosmetic lotion
	Paper adhesive
	Doughnut glaze
	Chocolate candy
	Cake frosting
	Skin disinfectant
	Hand lotion
	Hair lacquer
	Liquid face powder

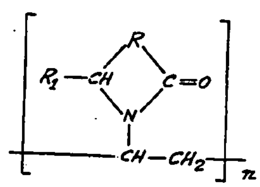
Exemplary plasticizing agents include unsaturated fatty acids, unsaturated fatty alcohols, ethers of unsaturated alcohols, partially acetylated glycerides and the like, e.g., included are the following: linoleic acid, oleic acid, linolenic acid, "Myvacet 7—00" (a partially acetylated monoglyceride. Distilled Product Industries). "Myvacet" is a Trade Mark.

The water soluble N-vinyl lactam monomer and the polymer derived therefrom as employed herein have the formulae:

I.

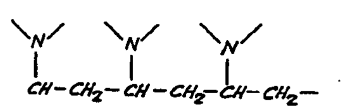


II. (when homopolymerized)



wherein R represents an alkylene bridge group necessary to complete a 5, 6 or 7 membered heterocyclic ring system. R_1 represents either hydrogen or an alkyl group, and *n* represents a number indicative of the extent of polymerization and is usually at least 3 or 4, when homopolymerized.

All of the specific polymeric materials characterized by the foregoing general formulae are commercially available and called polymeric N-vinyl lactams. They are obtained by polymerizing organic 5, 6 or 7-membered ring compounds containing in their rings the —NH—CO-group, such as i.e., 1 - vinyl - 2-pyrrolidone, 1 - vinyl - 5 - methyl - 2-pyrrolidone, 1 - vinyl - 2 - piperidone, N-vinyl - e - caprolactam, and the like. Depending upon the extent of polymerization, they generally have molecular weights ranging from 400 up to 2,000,000. Viscosity measurements are commonly used as an indication of the average molecular weight of polymeric compositions, the present polymers being characterized by a chain of carbon atoms to which the lactam rings are attached through their nitrogen atoms:



The K value (Fikentscher) of any particular mixture of polymers is calculated from viscosity data and is useful as an indication of the average molecular weight of such mixture. Its determination is fully described in "Modern Plastics," 23, No. 3,157—61,212, 214,216,218 (1945), and is defined as 1000 times k in the empirical relative viscosity equation:

$$\frac{\log_{10} n_{rel}}{C} = \frac{75^2 + k}{1 + 1.5\,kc}$$

wherein C is the concentration in grams per hundred cc. of polymer solution and n_{rel} is the ratio of the viscosity of the solution to that of pure solvent. The K values are reported as 1000 times the calculated viscosity coefficient in order to avoid the use of decimals. For the purpose of the present invention, there may be employed those polymeric N-vinyl lactams having a K value of 10 to 100, preferably of 15 to 90. If emulsions of higher viscosity are desired without increasing melt solids, polymers having a higher molecular weight may be employed, such as for the melt mix preparation.

K values and specific viscosities (n_{sp}) are interconvertible and are related through relative viscosity (π_{rel}). Thus, when viscosity measurements are taken on solutions which have a concentration of 1.00 gram of polymer per deciliter of solution at 25° C. (c=1), the relationships are as follows:

$$\pi_{rel} = n_{sp}\ 1$$

Relative viscosity = specific viscosity plus one.

Relative viscosity =
$$10[0,001K + 0.000075K^2/(1+0.015K)]$$

Hence, n_{sp} =
$$-1\ 10[0.001K + 0.000075K^2/(1+0.0015K)]$$

Relative viscosity, specific viscosity and K are dimensionless, whereas inherent viscosity

$$\frac{(\log_e n_{rel})}{C}$$

and intrinsic viscosity (the limit of inherent viscosity as C approaches zero) have the dimensions of dilution, i.e., the reciprocal of concentration.

The number of recurring polymer units enclosed by brackets in the foregoing general structural formula, indicated by "*n*," or the extent of degree of polymerization, corresponds to a chain of generally 4 to 20,000 monomer units. In actual practice, a mixture of poly-

meric molecules, each containing a different number (n) of monomer units, is always produced. The polymers are readily prepared by the procedural steps given in U.S. Patent Specifications 2,265,450, 2,317,804, and 2,335,454 and in which working examples of all the species characterized by the above formulae are given.

The ratio of the N-vinyl lactam to the plasticizing agent may be varied depending upon what type of melt blend or emulsion is desired. For example, melts having more than 50% by weight plasticizing agent form soft and more flexible films and thus are suitable for the coating of food substances or tablets. Melts prepared with high molecular weight polymeric N-vinyl lactams for strong and more rigid films are more easily pulverized. The thickness of the emulsion is a function of the quantity of melt to solvent; rather than the amount of polymer in the melt. In the same manner, the emulsion viscosity may be kept quite low so as to enable it to pass through the nozzle of an aerosol spray can.

Broadly speaking, one aspect of the invention comprises blending the poly (N-vinyl lactam) (PVL), such as for instance, poly (N-vinyl pyrrolidone) or copolymer of an N-vinyl lactam and vinyl acetate melt in hot water while vigorously mixing, thereby resulting in a melt-water emulsion. The quality of emulsion will depend on the temperature of the water, agitation and the type of melt. Water-melt emulsions can be prepared either directly by adding the hot melt to hot water or indirectly by adding pulverized melt material into hot water. Melts can also be emulsified in lukewarm or cold water; however, this method takes a longer period of time and requires more mechanical stirring. Furthermore, such emulsions (the latter) are not as stable as emulsions prepared at 90—100° C. (they tend to separate more quickly).

Preferably the components blended in hot melts or entrapped in cold melt matrixes are emulsified together with the melt. The physical properties of such emulsions will depend on the ratio of melt to water and the type and amount of unsaturated fatty material used in the original melt. Emulsions containing 40 or more percent by weight of emulsified melt can be considered heavy viscosity lotions or creams. Emulsions containing less than 40% by weight solids will be considered liquid lotions or low viscosity aqueous emulsions.

Emulsion stability' and emolliency characteristics will definitely depend on the type of melt that is being emulsified. A "melt" composed of a poly (N-vinyl lactam) and partially acetylated glycerides or fatty acids will form better emulsions than the one made from the corresponding alcohols or ethoxylated alcohols. Branched chain fatty acids form better emulsions than linear analogues of the same fatty acids; also unsaturated fatty acids form better emulsions than the saturated acids. Emulsion stability, emolliency and the like also depend on the poly (N-vinyl lactam)—unsaturated fatty component ratio in the melt. The best emulsions are obtained when the unsaturated fatty component concentration is the same as or less than the concentration of poly (N-vinyl lactam) or copolymer. Melts having a high concentration of the "fatty" component do not form stable emulsions. Thus stable emulsions are obtained when the composition of the melt preferably is 40—80% poly (N-vinyl lactam) or a copolymer of VP/VA and 60—20% unsaturated fatty component.

best

As with poly (N-vinyl lactam) or copolymer melts, melt emulsions are primarily designed for pharmaceutical and veterinary applications. However, they can be useful in: (1) the food industry, especially in the treatment of cereal and (flour) baked food stuffs, (2) cosmetic-emulsions can be used (directly or modified) as moisturizing, conditioning skin preparations in the form of lotions or creams; also emulsions are good opacifying compounds for various cosmetic preparations such as cream rinses, cream conditioners, etc.

Additional applications include:

1. Various pharmaceutical components such as vitamins, aspirin, MgO, etc., can be entrapped in safe and stable emulsions.
2. Components entrapped in melt emulsions may mask unacceptable odour or taste.
3. Vitamins and other nutritive agents can be embedded in melts.
4. Emulsions so prepared can thereafter be sprayed on cereal and other food stuff.
5. Melt emulsions should be acceptable to U.S. Food & Drug Administration for use in edible mixtures.
6. Melt emulsions can be applied as a cream or lotion by itself, or formulated with other components.
7. Emulsions can be used as safe opacifiers in food, beverage, or cosmetic applications.

One may employ 70 parts by weight of poly (N-vinyl lactam) or copolymer to about 30 parts by weight of plasticizing agent, however, the ideal ratio is 55—45. In the emulsion, the weight ratio may be 1:1:98 (PVL/Plasticizer/water) to 40:40:20 (PVL/Plasticizer/water).

The present invention may comprise, as the principle substituents of formulation, therapeutic ingredient(s) distributed throughout a molecularly dispersed poly (N-vinyl lactam) or copolymer phase, and forming a network about a water insoluble, hydrophobic, unsaturated fatty acid or fatty acid component macrophase, the poly (N-vinyl lactam)-fatty acid constituents being in the ratio of 0.5:1 to 4:1 of poly (N-vinyl lactam): plasticizing agent when employed in the form of the melt.

The active component may be dissolved or lactam)-plasticizing mass just before the mass is removed from heating. Upon cooling, the molten mass forms a solid film which may later be granulated into a powder or directly emulsified. It will be observed that the ratio of poly (N-vinyl lactam) or copolymer to unsaturated acid component is not critical, and may be varied over a substantial range, depending upon the rate of release of the active component desired. When the above weight ratio is from 1 to 0.5 to 1, release of the active ingredient is obtained in approximately a couple of hours. When the ratio is 1 to 1.5 to 2.0, the incorporated active ingredient is released over a longer period of time, approximately over five hours. When the ratio is from 1 to 3 to 4, release is obtained over a much longer period of time, approximately 12 to 24 hours. Of course, all the foregoing times may be affected by a variety of variables, such as ingredient, variation of components and the like.

Although the mechanism whereby gradual release of the active ingredient is attained over an extended time period from the novel combination of this invention has not absolutely been determined, it is believed with reasonable certainty that the desired effect is achieved because of the peculiar physical combination of components, compatability, insolubility parameters and a co-action during absorption on the surface to which same has been applied.

When preparing the emulsion, the combination of the present invention comprises, in a general way, the addition of the melt to a sufficient volume of water to wet (disperse or emulsify) the dry melt containing the prescribed quantity of unsaturated fatty acid component-poly (N-vinyl lactam) or copolymer and active ingredient as well as any other constituents, if desired. The active ingredient dissolved in the added water, when water soluble, becomes evenly distributed throughout the poly (N-vinyl lactam) or copolymer aqueous phase. On the other hand, where the active ingredient is insoluble in water it will become dispersed throughout the non-aqueous phase with the unsaturated fatty acid component. The active ingredient-poly (N-vinyl lactam) or copolymer water system will flow easily about the hydrophobic fatty acid microparticles. On the other hand, the active ingredient-hydrophobic unsaturated fatty acid component micro particles will be evenly dispersed throughout the poly (N-vinyl lactam) or copolymer aqueous system.

When the above described composition comes in contact with the digestive juices, the aqueous medium infiltrates the hydrophobic fatty acid component mass at a slow, constant rate by following the network path of the hydrophilic copolymeric film through capillary action. The molecules of reactive ingredient are dissolved in the digestive juices at the point of contact of the latter with the drug containing polymeric film. The dissolved active ingredient is then free to diffuse into the body and the surrounding area and is available for absorbtion. Because of this method of diffusion of drug out of the emulsion there is no rupture of the fatty acid mass, and the composition is operative to function as an inert carrier for the active ingredients.

It should be borne in mind that whether by solid or by emulsion, there are essentially two competing forces operating within this composition as it travels the intestinal tract and is bathed in the aqueous fluid, namely, the hydrophobic barrier of the unsaturated fatty acid component and the surrounding hydrophilic film of the polymer and active component. As a result, the dissolution of water soluble therapeutics is readily controlled by increasing or decreasing the quantity of hydrophobic material in the composition. In other words, by adding a relatively high proportion of fatty acid component, as compared to polymer, the active ingredients will be released over a long period of time. Conversely, by decreasing the ratio, the therapeutic component is released over a shorter period of time. Advantage is thus taken of the unique hydrophilic, nonswelling film forming properties of the poly (N-vinyl lactam) or copolymer thereof as contrasted to the action of other commonly used components which do not possess such physical properties. It should also be borne in mind that where the active ingredient is not water soluble, the unique ability of the polymer to complex with the fatty acid component and thus produce an emulsion therefrom affords the composition the opportunity to remain substantially uniformly dispersed throughout an emulsified phase wherein the active ingredient is in the non-aqueous phase.

It will be readily apparent, therefore, that the novel composition herein lends itself to a wide variety of applications in the pharmaceutical field since it provides a method for administering water-soluble and water-insoluble therapeutics singly or in admixture with other substances, over a controlled period of time with predictable regularity and time lag. Drugs which are suitable for use in the novel composition include antihistamines, central nervous system depressants, central nervous system stimulants, vitamins, antibiotics, antacids, cough depressants, etc. These may be incorporated into the novel composition either in the form of water-insoluble bases or as their water-soluble salts, depending upon the particular mode of absorption found most advantageous.

There is no restriction on the inclusion of other commonly employed excipients in the formulation of the novel combination of this

invention. Thus, one may employ as diluents in whatever quantities are indicated, such components as dibasic calcium phosphate, lactose, mannitol, and thers. One may also include as binders, such gums as acacia, or tragacanth.

The following examples are intended to illustrate but not to limit the scope of the present invention. All parts and proportions herein as well as in the appended claims are by weight unless otherwise indicated.

GENERAL PROCEDURE FOR PREPARING MELTS.

The plasticizing agent (fatty alcohol-unsaturated fatty acid-, partially acetylated glyceride, or ethoxylated fatty alcohols or mixtures of these components) is heated to 120—150° C., a polymeric N-vinyl lactam (PVL), e.g., a polymeric N-vinyl pyrrolidone (PVP, K 29—32, K—30, or 90) or VP/VA copolymer is slowly added while stirring. When all of the polymeric lactam is added, stirring is continued for several more minutes, then the component to be imbedded is added to the molten mass, stirred several minutes longer, transferred to a dish or pan and allowed to cool. The solid matrix is then broken up into smaller pieces and pulverized on the mill. The composition of the melt can be summarized in the following formula:

PVP or copolymer of VP/VA	40—80 parts
Plasticizing component	20—60 "
Active component	0.05—50

It is difficult to dissolve greater than 70 parts of PVP alone or VP/VA into 30 parts of plasticizing agent. The ideal ratio, therefore, is 55 parts of PVP to 45 parts of plasticizer.

The copolymer of vinyl pyrrolidone and vinyl acetate may be prepared in accordance with techniques known in the art.

PREPARATION OF MELT EMULSIONS.

1. *Hot Melt to Hot Water Procedure*

A quantity of distilled water is brought to boil, 80 gm. thereof is weighed into a beaker and then transferred to a Waring blender jar which is heated by a heat gun directed at the base of the jar. 20 gms. of hot melt (100° C. or over) is transferred to the rapidly agitating Waring blender and stirring is continued for 10 minutes. The Waring blender is then stopped and the emulsion transferred to a jar.

PULVERIZED MELT TO HOT WATER.

The procedure for preparing emulsions from powdered solids is similar to that above. Instead of adding hot melt, pulverized material is added slowly while vigorously mixing under constant heat. When all the pulverized material has been added, stirring is continued for 10 more minutes. The emulsified material is then transferred to a jar.

COMPARATIVE EXAMPLES.

Investigation of PVP-Stearyl Alcohol Melt Characteristics.

Example A

7 gm. Polyvinyl pyrrolidone (PVP) is dissolved in melted stearyl alcohol (63 g.) with stirring until it congeals. The congealed mass is cooled to room temperature, broken up and passed through a No. 10 mesh screen and No. 10 mesh screen and No. 16 mesh screen (U.S. Standard mesh sizes).

Example B

The procedure of Example A is repeated with twice the amount of PVP, leaving the amount of stearyl alcohol the same. Ratio—1:4.5 PVP: stearyl alcohol.

Results: PVP dissolves readily at 70° C. Half a portion of this melt is allowed to solidify; the other half is further heated to 145° C. then allowed to cool. The melt mass appeared to be homogeneous at both temperatures.

Example C

A PVP-stearyl alcohol ratio of 1:2.25 is used. The PVP herein did not melt as readily and completely at 70° C. The 70° C. melt matrix herein is a slurry of unmelted granular PVP in stearyl alcohol. The PVP melt at 140° C. temperature is homogeneous in the molten and solid state.

Example D

A PVP-stearyl alcohol ratio of 1:1 is used. At 70° C. only a portion of PVP melt material appears to be compatible in the slurry. A cooled melt-matrix contains a large portion of granular PVP.

At 140° C. all PVP melts and forms a homogeneous, transparent mass. Upon cooling, it forms a smooth, translucent matrix.

Compatability data of PVP-stearyl alcohol melts with a candelilla wax ratio of 7:8 PVP melt: candellila wax at 80° C. is found below.

TABLE I

PVP/Stearyl Alcohol Ratio	PVP Melt Preparation Temp., °C.	Compatability Data of PVP Melt and Candililla Wax
1:9	70	compatible
1:9	140	,,
1:4.5	70	,,
1:4.5	140	,,
1:2.5	70	incompatible
1:2.5	140	,,
1:1	70	,,
1:1	140	,,

Preparation of PVP-stearyl alcohol emulsions from PVP melts are described in Table II.

TABLE II

PVP/Stearyl Alcohol Ratio	PVP Melt Preparation Temp., °C.	Appearance of Emulsion
1:9	70	Did not form emulsion. Two separate layers.
	140	Same as above
1:4.5	70	Same as above
	140	Same as above
1:2.5	70	Some emulsified product but bulk of stearyl alcohol precipitated.
	140	Same as above
1:1	70	Same as above
	140	Completely homogeneous and smooth emulsion.

Example 1

Partially acetylated monoglyceride ("Myvacet" 7–00)	45 g.
PVP K 29–32	55 g.
Vitamin "C" (Merck)	10 g.

Melt Preparation

A beaker containing the plasticizer ("Myvacet") is placed into an oil bath. The plasticizer is heated to 145—153° C., the PVP is sifted into the plasticizer over a 10 minute period while stirring constantly. It is allowed to stand for about 2 minutes, the vitamin is then added over a 1—2 minute period. The mixture is immediately cast as a film onto a "Mylar" sheet and allowed to cool. The thus formed melt is broken into small pieces and placed into a blender along with a small quantity of dry ice. "Mylar" is a Trade Mark. The melt was ground for several minutes or until it becomes granular or powdery. It was transferred to a petri dish, and placed in a desiccator to dry the contents and to prevent moisture formation.

PREPARATION OF MELT EMULSION.

A blender jar is placed on the blender base and a heat gun directed to the base of the jar. A 10 gm. portion of pulverized melt is weighed out and set aside. A flask containing distilled water is heated to the boil, 40 gms. of boiling water are then transferred immediately to the blender jar. Portions of the pulverized melt are added step-wise, mixing after each addition, until all the pulverized melt has been added. The blender is run for about 10 minutes after the melt addition is completed.

The temperature of the emulsion is about 80° C. after mixing.

Example 2.

The procedure of Example 1 is followed for both the preparation of the melt and emulsion. The ingredients of the melt are varied as follows:

Stearic Acid (food grade)	45 g.
PVP (K=29—32)	55 g.
Riboflavin (Merck)	1 g.

Example 3.

The procedure for the preparation of the emulsion is the same as in Example 1, for the melt it is similar except that the acetylsalicylic acid and the phenacetin are added over a five minute period.

Stearic Acid (food grade)	22.5 g.
PVP (K=29—32)	27.5 g.
Acetylsalicylic Acid	12.5 g.
Phenacetin	7.5 g.

Example 4.

The procedure for the preparation of the emulsion is the same as in Example 1, for the melt it is similar except that the zinc oxide is added over a 4 minute period.

Stearic Acid (food grade)	45 g.
PVP (K=29—32)	55 g.
Zinc Oxide	10. g.

Example 5.

The procedure of Example 1 is followed for both the preparation of the melt and emulsion. The ingredients of the melt are varied as follows:

Partially acetylated monoglyceride (" Myvacet ")	45 g.
PVP (K=29—32)	55 g.
Thiamin (Merck)	10 g.

Example 6.

The procedure of Example 1 is followed for both the preparation of the melt and emulsion. The ingredients of the melt are varied as follows:

Partially acetylated monoglyceride (" Myvacet ")	45 g.
PVP (K=29—32)	55 g.
Magnesium Oxide (Heavy USP)	10 g.

Example 7.

Preparation same as in Example 6 except that there is added 10 g. wild cherry syrup to a portion of the emulsion.

Example 8.

The procedure of Example 1 is followed for both the preparation of the melt and emulsion. The ingredients of the melt are varied as follows and they are pulverized using a Wiley Mill.

Stearic Acid	45 g.
PVP (K=29—32)	55 g.
Cyanocobalamin (Vitamin B_{12}), (Merck)	1 g.

Example 9.

The procedure of Example 1 is followed for both the preparation of the melt and emulsion. The ingredients of the melt are varied as follows and they are pulverized using a Wiley Mill.

Stearic Acid	45 g.
PVP (K=29—32)	55 g.
Aquapalm (Vitamin A Palmitate), (Hoffman - La Roche)	1 g.

Example 10.

The procedure of Example 1 is followed for both the preparation of the melt and emulsion. The ingredients of the melt are varied as follows and they are pulverized using a Wiley Mill.

Stearic Acid	45 g.
PVP (K=29—32)	55 g.
di-*Alpha* Tacophenyl Acetate NF—FCC (Vitamin E Acetate) (Hoffman-La Roche)	1 g.

Example 11.

The procedure of Example 1 is followed for both the preparation of the melt and emulsion. The ingredients of the melt are varied as follows:

Partially acetylated monoglyceride (" Myvacet ')	60 g.
PVP (K=90)	40 g.

Example 12.

The procedure of Example 1 is followed for both the preparation of the melt and emulsion. The ingredients for both are varied as follows:

Stearic Acid	70 g.
PVP (K=90)	30 g.

Example 13.

The procedure of Example 1 is followed for both the preparation of the melt and emulsion. The ingredients for both are varied as follows:

Partially acetylated monoglyceride ("Myvacet")	45 g.
Copolymer of vinyl pyrrolidone/vinyl acetate (PVP/VA)	55 g.

Example 14.

The procedure of Example 1 is followed for both the preparation of the melt and emulsion. The ingredients for both are varied as follows:

1-Octadecanol	50 g.
PVP (K=30)	50 g.

Example 15.

The procedure of Example 1 is followed for both the preparation of the melt and emulsion. The ingredients for both are varied as follows:

*Iso*stearic Acid	45 g.
PVP (K=29—32)	55 g.

Example 16.

The procedure of Examples 1—10 is followed for the preparation of the melt except oleic acid is used instead of ("Myvacet"). The procedure for the emulsion is as follows:

Bring a quantity of distilled water to boil, weigh out 400 g. thereof and transfer to a preheated blender jar. Add the hot melt directly to the water and mix for 10 minutes and thereafter transfer the emulsion to a clean jar.

Oleic Acid	45 g.
PVP (K 29=32)	55 g.

Example 17.

The procedure of Example 1 is followed for the preparation of the melt except isostearic acid was used instead of (Myvacet 7—00). The procedure for the emulsion is the same as that followed in Example 16 but with the use of 150 g. H_2O (40% Emulsion-thicker and creamier than Example 16—20% Emulsion).

*Iso*stearic Acid	45 g.
PVP (K 29=32)	55 g.

Example 18.

The procedure for the preparation of the melt is the same as in Example 1 except oleic acid was used instead of (Myvacet). The procedure for the emulsion is the same as that followed in Example 16 but with the use of 66 g. H_2O (60% Emulsion—very thick, creamy, smooth).

Oleic Acid	45 g.
PVP (K=29—32)	55 g.

Example 19.

Method for opacification of Cream Rinse:

Formula	Wt.%
Quaternized polyvinyl pyrrolidone dimethylaminoethylmethacrylate copolymer 80/20 in alcohol solvent	0.50 (100% Solids)
Ethoxylated lanolin alcohol (100 moles E.O.)—("Ethoxylan 100"—Malmstrom)	0.15
Ethanol SDA—40	15.00
Methyl paraben USP	0.10
Distilled H_2O	82.25
Emulsion, 60% (Ex. 18)	2.00
	100.00

The resultant emulsion gives a milky appearance to cream rinse.

Example 20.

Method for opacification of conditioner:

Formula	Wt.%
Quaternized polyvinyl pyrrolidone/dimethylaminoethylmethacrylate copolymer 80/20 in water solvent	1.55 (100% Solids)
Ethoxylated isostearyl alcohol (10 moles E.O.) ("Emulphor AM—650"). ("Emulphor" is a Trade Mark.)	0.08
Dimethylpolysiloxane / polyethylene oxide-polypropyleneoxide copolymer (Silicone SF—1066—G.E.)	0.08
Perfume IFF No. 3159—E	0.10
SDA—40	32.90
Disodium salt of 4 - {[4 - (N - ethyl - *p*-sulphobenzylamino)phenyl] (2 - sulphoniumphenyl)methylene} [1 - N - ethyl-N - *p* - sulphobenzyl) - $^{\Delta 2,5}$ - cyclohexadienimine ("FDC" Blue No. 1, 0.6% H. Kohnstamn & Co.)	0.10
Stearyl dimethylbenzyl ammonium chloride ("Ammonyx 490—Oxyx Chemical Co.)	0.10
Distilled H_2O	63.09
Emulsion, 60% (Ex. 18)	2.00
	100.00

The addition of a quantity of emulsion as produced in Ex. 18 renders the clear conditioning setting lotion opaque.

Example 21.

Formula for Moisturizing Cream for Dry Skin

Formula	Wt.%
60% Emulsion (Ex. 18)	100 g.
Multi-sterol non-ionic emollient. Sterol anl higher alcohols are present only in their free forms ("Amerchol L—100—A—)	25 g.
*Iso*propyl ester of highly purified lanolin fatty acid. (Amerlate P)	3 g.
Dimethylpolysiloxane / polyethylene oxide-polypropylene oxide copolymer (Silicone SF—1066—G.E.)	1 g.
Perfume	q.s.
Preservative	q.s.

Procedure: Weigh 100 g. of emulsified product from Ex. 18. Thereafter add Amerchol L—101, Amerlate P, and Silicone SF—1066 while slowly mixing. Add perfume and preservative.

Example 22.

Similar to Ex. 16 except with a substitution of linoleic acid for the oleic acid.

Example 23.

Similar to Ex. 16 except with a substitution of linolenic acid for the oleic acid.

The terms "unsaturated fatty acid component, unsaturated fatty component, and fatty acid component" as employed herein are intended to generically include any of the plasticizing agents operative herein, except when mentioned for comparative purposes.

Proof of Complex Formation by Infra Red Spectrophotometry.

In order to establish a formation of a complex between PVP (K=30)-fatty acid, alcohols, partially acetylated monoglycerides, etc., infrared examination was made using alcohol and chloroform solutions and physical blends of PVP-fatty compounds, to establish if there was any frequency shift.

All samples in Table III, except sample 1, are a 30% solution in undenatured alcohol or chloroform, of a mixture of 45% each of the various fatty acids, or alcohols a partially acetylated monoglyceride and 55% PVP (K—30). The solutions are prepared by adding separately the PVP and the other component to the solvent.

Sample 1 is a reference standard consisting of a solution in undenatured alcohol of PVP (K=30) only.

Infrared spectrum was obtained on each sample in Table 3 in the liquid (solution) and solid state (film). The film is obtained by evaporating the solution on a CsBr window at 100° C., for five minutes in a vacuum oven.

The reference sample 1 of PVP (K=30)

shows no shift in frequency (actual position of absorption band cm.$^{-1}$) when recorded as a solution or film while all the other samples[1] exhibit a change in frequency when recorded as films.

Samples in Table IV were prepared by the KBr technique; i.e. the sample is finely ground and mixed with KBr (powder), then compacted under pressure to form a clear pellet.

A reference sample of PVP (K—30) alone absorbs at 1650 cm^{-1}. PVP (K=30) itself, also absorbs at 1650 cm^{-1}.

An external blend, by Waring blender of 45% stearyl alcohol and 55% PVP (K=30) also absorbs at 1650 cm^{-1} but a similar blend prepared by melting the tw components absorbs at a higher frequency (1600 cm^{-1}).

A melt blend of various concentrations of Myvacet 7—00 and PVP (K=90) shows an increase in frequency as the PVP (K=90) concentration increases.

At the 100% PVP (K=90) level there is no frequency shift.

[1]Except isostearyl alcohol+3 E.O. om $CHCl_3$.

TABLE III

Infrared Spectroscopy Data of PVP/Plasticizer Blends

Sample	Description	Solvent	Position of Absorption Bands[2] Solution cm^{-1}	Position of Absorption Bands[2] Film cm^{-1}
1.	PVP (K=30) (100%)	Ethanol[1]	1652	1651
2.	Stearic acid + PVP (K=30)	,,	1650	1669
	*Iso*stearic acid + PVP (K=30)	,,	1650	1662
	Oleic acid + PVP (K=30)	,,	1650	1668
	Linoleic acid + PVP (K=30)	,,	1650	1660
	Myristic acid + PVP (K=30)	,,	1650	1661
3.	Stearyl alcohol + PVP (K=30)	,,	1650	1653
	*Iso*stearyl alcohol + PVP (K=30)	,,	1650	1660
	Cetyl alcohol + PVP (K=30)	,,	1650	1660
	Oleyl alcohol + PVP (K=30)	,,	1650	1660
	*Iso*stearyl + 1 E.O. + PVP (K=30)	,,	1650	1660
	*Iso*stearyl + 3 E.O. + PVP (K=30)	,,	1650	1665
	*Iso*stearyl + 5 E.O. + PVP (K=30)	,,	1650	1662
4.	"Myvacet" 7–00 + PVP (K=30)	,,	1650	1662
5.	Stearic acid + PVP (K=30)	$CHCl_3$	1655	1670
	Linoleic acid + PVP (K=30)	,,	1652	1663
	*Iso*stearyl alc. + 3 E.O. + PVP (K=30)	,,	1652	1645
	"Myvacet" 7–00		None	None

[1] undenatured alcohol

[2] –CON–band of PVP (K=30)

TABLE IV

Infrared Spectroscopy Data on PVP/Plasticizer Physical and Melt Blends Employing KBr Technique

Sample	Description	Position of Absorption Band (cm^{-1})[1]
6.	Melt blend of 45% stearyl alcohol + 55% PVP (K=30)	1660
7.	PVP (K=30)	1650
	PVP (K 29-32)	1650
8.	External blend, Waring blender, 50% stearyl alcohol + 55% PVP (K=30)	1645
9.	External blend, Waring blender, 45% stearyl alcohol + 55% PVP (K=30)	1650
10.	Melt blend of 90% "Myvacet"* 7–00 + 10% PVP (K=90)	1640
	" " 80% " " + 20% " "	1649
	" " 70% " " + 30% " "	1660 } complexing
	" " 60% " " + 40% " "	1661 } complexing
	" " 0% " " + 100% " "	1640

[1]–CON–band of PVP (K=30) or (K=90) comparable with film values of Table I

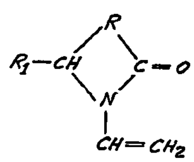
*Distilled Acetylated Monoglyceride derived from hydrogenated lard in which about 2/3 of the free OH groups are acetylated. Distillation Products Industries, Division of Eastman "Kodak" Company. "Kodak"/DPI Product Bulletins A–1 (6/15/72) and ZA–22 (1969)
"Kodak" is a Trade Mark.

It can be concluded from the data in Tables III and IV that some complexing results between mixtures of PVP and various compounds such as fatty alcohols, oxyethylated alcohols, fatty acids, partially acetylated monoglycerides. No complexing takes place in externally blended PVP/fatty acid films made from solutions and samples which have been merely blended (Table III and Table IV).

Furthermore, as can readily be determined from working Examples 1—6, a complex is formed at a temperature above 100° C., about 130° C., to which the fatty acid or fatty derivative is heated prior to the addition of the poly (N-vinyl pyrrolidone). As was readily apparent, where there is no heating above 100°, there occurred no complexing between the fatty acid and the poly (N-vinyl-pyrrolidone). Furthermore, the stable aqueous emulsions are formed from the most unsaturated acids, e.g. linoleic acid, linolenic acid, oleic acid, lastly the poorest emulsions were formed from the saturated fatty acid and fatty acid derivative.

WHAT WE CLAIM IS:—

1. A composition comprising by weight:
(a) 40 parts to 80 parts of a polymer, the polymer comprising (1) a homopolymer of an N-vinyl lactam of the general formula:



wherein R represents an alkylene radical of 2 to 4 carbon atoms and R_1 represents either hydrogen or an alkyl group, or (2) a copolymer of the said N-vinyl lactam with up to 70 percent vinyl acetate based on the weight of the said copolymer;
(b) 60 to 20 parts of a plasticizer;
(c) 0.05 to 50 parts of a medicinally active ingredient and
(d) 0 to 99 parts of solvent for components (a), (b) and (c).

2. A composition according to Claim 1, wherein the polymer has a K value of 10 to 100.

3. A composition according to Claim 1 or Claim 2, wherein the polymer is a copolymer composed of 50 to 90 percent by weight of the N-vinyl lactam and 50 to 10 percent by weight of the vinyl acetate.

4. A composition according to any preceding claim, wherein the N-vinyl lactam is N-vinyl pyrrolidone.

5. A composition according to Claim 1 or Claim 2, wherein component (a) is poly (N-vinyl pyrrolidone).

6. A composition according to any preceding claim, wherein component (b) is chosen from unsaturated fatty alcohols, unsaturated fatty acids, partially acetylated monoglycerides and ethoxylated fatty alcohols.

7. A composition according to Claim 6, wherein component (b) is selected from linoleic, linolenic and oleic acids.

8. A composition according to any preceding claim, wherein component (d) is present and is water.

9. A composition according to any preceding claim, wherein component (c) is therapeutically active.

10. A composition according to any preceding claim, wherein component (c) is water-soluble.

11. A stable aqueous emulsion derived from the composition as defined in any preceding claim.

12. A composition according to Claim 1 substantially as herein described with particular reference to any one of Examples 1 to 23.

13. A process of preparing the composition defined in Claim 1, wherein components (a), (b) and (c) with or without component (d) as defined in Claim 1 are heated to form a molten mass, thereafter allowing the mass to cool.

14. A process of preparing the composition defined in Claim 1, which comprises heating component (a) and thereafter adding components (b) and (c) and optionally (d).

15. A process according to Claim 13 or Claim 14, wherein the heating is carried out at a temperature between 100° C. and 150° C.

16. A process according to Claim 13 or Claim 14 substantially as herein described and exemplified.

17. A composition which has been prepared by the process claimed in any one of Claims 13 to 16.

18. An aerosol spray containing a propellant and a composition as defined in any one of Claims 1 to 10 or Claim 12.

19. A skin cream containing an emollient and a composition as defined in any one of Claims 1 to 10 or Claim 12.

20. A composition according to any one of Claims 1 to 10 or Claim 12, which becomes molten at a temperature of 100°—150° C.

21. An aqueous emulsion according to Claim 11 substantially as herein described and exemplified.

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Printed for Her Majesty's Stationery Office by the Courier Press, Leamington Spa, 1976.
Published by the Patent Office, 25 Southampton Buildings, London, WC2A 1AY, from which copies may be obtained.